DSH PSYCHOTROPIC MEDICATION Operational Procedures

BREXPIPRAZOLE PROTOCOL:

I. Indications:

A. At least one of the following clinical indications is present and documented in the chart:

1. DSM diagnosis of schizophrenia, schizoaffective disorder or other psychotic disorder (e.g., major depression with psychotic features). Also, may adjunctively assist in depression treatment.

2. Treatment of agitation associated with dementia due to Alzheimer's disease

3. DSM diagnosis of bipolar I disorder for acute treatment during a current episode, manic or mixed (if used beyond three weeks, long-term usefulness is reevaluated).

4. Severe persistent aggression or self-injurious behavior with evidence that a behavioral treatment, as part of a formal treatment program, was adequately implemented and found to be ineffective.

B. Contraindications:

Hypersensitivity to brexpiprazole or any component of its formulation.

II. Precautions (risk/benefit analysis supports use):

A. Signs or history of tardive dyskinesia.

B. Pregnancy or breast feeding. May cause neonatal dyskinesia.

C. Elderly patient with neurocognitive disorder-related psychosis.

D. History of leukopenia or severe neutropenia. The risk is low for brexpiprazole; however, the U.S. Food and Drug Administration has mandated a class warning for the second/third-generation antipsychotics.

III. The following initial workup should be completed:

A. There is informed consent or alternate legal authorization.

B. There is chart documentation of:

1. Waist circumference.

2. Personal or family history of diabetes.

3. Personal history of high BMI (>25).

4. Personal history of elevated triglycerides or hypercholesterolemia.

C. Initial workup includes:

1. Fasting blood glucose and/or Hgb A1c (optional within 30 days).

2. Lipid panel or total cholesterol and triglycerides within 30 days.

3. AIMS rating within one year.

4. ECG within one year.

IV. Monitoring:

A. Monthly monitoring includes weight/BMI.

B. Semi-annual monitoring includes:

1. Fasting serum glucose and/or Hgb A1c (optional).

2. Lipid panel and/or triglycerides and cholesterol.

C. Annual monitoring includes waist circumference, ECG, and AIMS.

D. Positive AIMS results in quarterly monitoring, until negative twice.

E. Fasting serum glucose levels of 100 mg/dL or higher or elevated Hgb A1c result in glucose tolerance test or 2-hour postprandial blood glucose measurement and medical consultation.

F. Nutritional consultation and appropriate dietary and exercise interventions are pursued if any of the following weight gain indicators occurs:

1. Weight % increase of 5% in one month, 7.5% in three months, or 10% in six months.

2. Waist circumference increase from below 35in. to > 35in. for females and from below 40in. to > 40in. for males.

3. BMI increase from normal to overweight (from <25 to >25) or from overweight to obese (from 25 – 29.9 to 30 or higher).

G. Abnormal or rising triglyceride and cholesterol levels result in medical consultation and appropriate interventions.

V. Dose initiation and titration:

A. Typical initial dose is 1 – 2 mg daily, with titration up to 3 mg per day for adjunctive treatment of depression and up to 4 mg per day for treatment of psychosis. Doses greater than 4 mg per day continued for more than 15 days require Medication Review Committee (MRC) or Therapeutic Review Committee (TRC) consultation or review.

In general, oral antipsychotics should be titrated upward every two weeks until one of four endpoints is reached, i.e., the desired clinical result is achieved, intolerable unmanageable adverse effects are encountered, the point of futility for the antipsychotic is reached, or an upper dose limit established by law or regulation is reached.

B. Dose accounts for drug-drug interactions:

1. Dose may require up to doubling if used with carbamazepine, a CYP3A inducer.

2. Dose may require increase if used with other CYP3A inducers (e.g., phenytoin, phenobarbital, primidone, oxcarbazepine or some glucocorticoids).

3. Dose may need to be up to halved if used with ketoconazole, a CYP3A and 2D6 inhibitor.

4. Dose may require decrease if used with other CYP2D6 inhibitors (e.g., paroxetine or bupropion) or with CYP3A inhibitors (e.g., erythromycin, cimetidine or fluvoxamine).

5. Lowest possible dose is prescribed if used with fluoxetine, a CYP2D6 and CYP3A inhibitor.

VI. Possible Adverse Reactions:

A. Headache.

B. Anxiety.

C. Insomnia.

D. Agitation.

E. Esophageal dysmotility.

F. Dyspepsia.

G. Nausea.

H. Vomiting.

I. Anorexia.

J. Constipation.

K. Light headedness.

L. Dizziness.

M. Seizures (one of lowest risks among antipsychotics).

N. Blurred vision.

O. Somnolence (one of lowest risks among antipsychotics).

P. Akathisia.

Q. Extrapyramidal signs.

R. Tardive dyskinesia.

S. Neuroleptic malignant syndrome.

T. Orthostatic hypotension (one of lowest risks among antipsychotics).

U. Weight gain or loss.

V. Hyperglycemia and diabetes mellitus.

References:

American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists & North American Association for the Study of Obesity 2004. Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care,* 27**,** 596-601.

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